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高载量层析介质的 tailor-made 策略及在复杂生物大分子分离纯化领域的应用研究*

赵岚 黄永东** 朱凯 吴学星 李强 苏志国 马光辉**

（中国科学院过程工程研究所，生化工程国家重点实验室，北京，100190）

摘要

层析技术在生物分离纯化领域占有非常重要的地位。作为该技术主要组成部分，层析介质的结构与性能极大地影响最终分离纯化效果。其中，载量是决定介质分离纯化能力的重要性质，如何提高介质载量是生物分离工程领域一直关注的重点。本论文以高载量琼脂糖层析介质为目标，分别开展了琼脂糖疏水层析介质和金属螯合层析介质的 tailor-made 研究。对于琼脂糖疏水层析介质，引入不同长度间臂，实现疏水性质可控制备，并用于 CHO 细胞表达乙肝表面抗原纯化，该方法能显著提高介质对疫苗的结合量，疫苗活性回收率达 90%以上，纯化倍数 65.8，均优于传统疏水介质。对于琼脂糖金属螯合介质，通过采取接枝葡聚糖策略，同时调控接枝程度，实现葡聚糖接枝可控制备。这种接枝型金属螯合介质对组氨酸标记重组蛋白的载量较传统介质提升 1.5 倍以上，远优于传统介质。Tailor-made

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**通讯作者，电子邮箱：ydhuang@ipe.ac.cn，ghma@ipe.ac.cn

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型高载量层析介质在重组蛋白大规模分离纯化领域前景广阔。

关键词

层析介质；高载量；tailor-made；间臂；葡聚糖接枝

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Tailor-made High-capacity Chromatographic Media and Its Applications in Purification of Complex Biomacromolecules

Lan Zhao Yongdong Huang Kai Zhu XingXing Wu Qiang Li

Zhiguo Su Guanghui Ma

State Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, PR China

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Abstract

Chromatography has been playing an important role in bioseparation. As one of the main components of chromatography, the structure and properties of chromatographic media have great effects on purification results. Among them, capacity is one of the most important properties to determine chromatographic media's purification effects, and how to improve the capacity is one of the key points having been paid close attention to in bioseparation. This paper is based on high-capacity agarose-based chromatographic media, with hydrophobic and immobilized metal ion affinity chromatographic media being tailor-made, respectively. For hydrophobic chromatographic media, various lengths of spacer arm were introduced with a controllable hydrophobic property, and the media was used in CHO-rHBsAg purification. rHBsAg binding capacity was greatly improved by this media containing spacer-arms, and rHBsAg recovery was more than 90% and the purification factor was 65.8, both higher than the results from traditional chromatographic media. For immobilized metal ion affinity chromatographic media, dextran molecules were grafted with manipulation and its capacity of His-tagged recombinant proteins was enhanced by 1.5 times than that of traditional media. This novel tailor-made high-capacity chromatographic media is promising for large scale purification of recombinant proteins.